Date: December 13, 2001

To: Members of the Orthopaedic and Rehabilitation Devices Advisory Panel (the Panel)

From: Hany Demian, M.S., Executive Secretary to the Panel
Restorative Devices Branch, Division of General, Restorative and Neurological Devices, Office of Device Evaluation, Center for Devices and Radiological Health

RE: InFUSE™ Bone Graft/LT-Cage Lumbar Tapered Fusion Device, P000058, a three-component spinal fusion device (consisting of a spinal fusion cage, a growth factor and a carrier) for the treatment of degenerative disc disease fro Medtronic Sofamor Danek

Dear Panel Member:

Thank you for agreeing to participate in the upcoming January 10, 2002, panel meeting and providing your support to ou program. Please remember that the information contained in this panel mail-out is confidential. Please do not discuss th information with any of your colleagues. Please remember to secure this information at all times.

Summary of the Device:

The device system you are being asked to review consists of multiple components and does not require the use of autograft bone. The three device components are 1) a tapered Ti alloy fusion cage; 2) a growth factor (recombinant human bone morphogenetic protein-2 [rhBMP-2]); and 3) a bovine collagen sponge carrier (absorbable collagen sponge [ACS]) to hold the growth factor. The rhBMP-2 is soaked into the ACS. This combination is then rolled and placed into the center of the fusion cage which is then implanted in the normal manner. The rhBMP-2 is intended to provide the appropriate signals to induce the formation of bone within the ACS. This newly formed bone is intended to solidify within the cage, as well as w the inferior and superior endplates, to form a fusion mass.

Panel Questions:

In a couple of weeks, we will send you the finalized panel questions to consider during your discussions relating to the devi system. These questions will focus on the following topics:

Issues related to the actual clinical performance of the device:

- the overall clinical behavior of the device system, including review of the adverse events
- the interpretation of the radiographic images (plain films and CT scans) in the absence of bone graft

Issues related to the use of growth factors in general:

- immune response(s) to the rhBMP-2/ACS device components and the potential for subsequent adverse events
- the potential tumorogenicity of the rhBMP-2/ACS device components
- the potential impact of the rhMBP-2 device component on women of child-bearing potential, reproduction and fet development

It is important to note that the growth factor questions are <u>not</u> based on any adverse events reported during the use of the device under review. While antibody assays were performed on all enrolled subjects, no adverse events related to these questions were reported, *e.g.* birth defects or cancer. These questions are based on non-clinical studies reported in the literature that indicate that the potential for these concerns exists.

You are being provided with the following information:

1. FDA review memos
   - overview memo of entire the PMA
   - preclinical summary memo
   - clinical summary memos
   - statistical summary memos

2. material from the sponsor

volume 1
- clinical data from the open surgical approach and control groups
- response to deficiency related to correlation between antibody levels and clinical outcome
- response to deficiency related success rate and fusion success based on plain films vs. CT scans
- investigational plan and case report forms
- statistical plan

volume 2
- clinical data from the laparoscopic surgical approach group
- sample labeling (package insert, surgical technique manuals and patient information brochure)
- summary of rhBMP-2 preclinical testing for use in the spinal fusions by the sponsor
- literature reports of the use of rhBMP-2 for spinal fusion

volume 3
- statistical analyses for all groups
- *This volume is only being provided to the clinical and statistical reviewers.*

volume 4
- summary of rhBMP-2 preclinical testing from Genetics Institute, supplier of the growth factor

Please note that the CDs containing plain film and CT images from investigational and control subjects will be provided only to the clinical and radiographic reviewers in a separate mailing.

If you have any general questions you may contact Mr. Hany Demian at (301) 594-2036, ext. 184; hwd@cdrh.fda.gov. If you have any questions regarding the PMA, please contact Mr. Aric Kaiser, the lead reviewer @ 301-594-2036 ext 158; adk@cdrh.fda.gov;

Again, I would like to thank you in advance for your participation in reviewing these important issues which will be discussed at the January 10, 2002, meeting of the Orthopaedic and Rehabilitation Devices Panel.

Sincerely yours,

Hany Demian, M.S.
Executive Secretary
Orthopaedic and Rehabilitation
Devices Panel